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09/471,669	12/24/1999	JOHN P. ANDERSON	00228-US-NEW	7795

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EXAMINER
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WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 05/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/471,669

Applicant(s)

ANDERSON ET AL.

Examiner

Malgorzata A. Walicka

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**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 21 April 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: \_\_\_\_\_.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see the attached.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

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Amendment filed April 21, 2006 and Terminal Disclaimer are acknowledged. Claims 1-47 have been withdrawn. Claims 49-50, and 70-113 have been previously canceled. Claims 48, 58, 64, 114, 122, 130, 138, 146, 154, 162, 170, 178, 184, 190, 196, 202, 208, 214, 220, 240, 259, 278, 297, 314, 333, 352 and 371 have been amended. Claims 48, 51-69, and 114-390 are pending and under examination.

The terminal disclaimer filed on April 21, 2006 disclaiming the terminal portion of any patent granted on this application which would extend beyond the last day of the full statutory term of the 09/724,569 application has been reviewed and is accepted. The terminal disclaimer has been recorded.

### **Advisory action**

#### **1. Rejections**

##### **1.1. 35 U.S.C. 112, second paragraph**

Claim 48, 114, 122, 131, 139, 147, 155, 163 and 171 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are still confusing.

Firstly, an isolated nucleic acid cannot comprise anything but a nucleotide sequence. The coma after "nucleic acid" in the first line is confusing. In the fourth line there is recitation "any such nucleotides" which is not correct, because a nucleotide sequence cannot be complementary to "such nucleotides", but to a nucleotide sequence. Nucleotides as such do not encode anything; see objections in the previous action. Only their sequence may encode something. It is understood that Applicant's intention is to claim one nucleotide sequence in each of the rejected claims, and not sequences as may be suggested by the plural form of nucleotide in "any of such nucleotides" at the end of the claim. In addition, the claims remain confusing in reciting the open language "comprising a sequence of nucleotides encoding beta secretase" and the closed language "the sequence of nucleotides consisting of".

Dependent claims 51-57, 115-121, 123-130, 132-138, 140-146, 148-154, 156-162, 164-170, 172-178 are included in the rejection because they do not correct the language of the claims from which they depend.

**Response to Applicants' arguments**

Applicants argue in their Remarks of April 21, 2006, page 30, third paragraph, and page 31, the claimed nucleotide sequences may include an initiation codon or a stop codon. They may also include regulatory sequences, a heterologous signal sequences or nucleotide sequences encoding an epitope tag to be used for purification, for example. The examiner agrees to this position, however, if Applicants intend to limit the scope of other sequences the claims encompass to these, the language of claims should explicitly state these limitations, and the current language does not do. The literary meaning of the language "sequence comprising a sequence consisting of a sequence encoding SEQ ID NO: 43" covers DNA molecules comprising a nucleotide sequence encoding SEQ ID NO: 43. One of DNA sequences comprising a sequence encoding SEQ ID NO: 43 has already been patented; see the rejection under 35 U.S.C. section 102 bellow. A suggestion for the alternative language of the rejected claims is "An isolated nucleic acid comprising a nucleotides sequence encoding the beta secretase consisting of SEQ ID NO: 43 or a perfect complementary sequence thereof."

**Also rejected are:**

claims 58-69

claims 178-183 and 240-258

claims 184-189 and 259-277

claims 190-195 and 278-296

claims 196-201 and 297-313

claims 202-207 and 314-332

claims 208-213 and 333-351

claims 214-219 and 352-370

claims 220-225 and 371-389.

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Claims 58, 178, 184, 190, 196, 202, 208, 214, 220 are confusing because the language "a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74" is confusing, rendering the claims confusing. One of skills in the art understands said language to mean that the vector comprises the nucleotides sequence consisting of the start codon before the first codon of the nucleotide sequence translated from amino acid sequence of SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74 and the stop codon immediately after the translated sequence; i.e., one of skills in the art understands that the expressed sequence will consists of SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74. However, a literary meaning of the language "a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74 " covers any DNA molecules comprising a nucleotide sequence encoding SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74. One of DNA molecules comprising molecules encoding SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74 has already been patented; see the rejection under 35 U.S.C. section 102 bellow. It is important to amend the language of the claims to be precise. As it stands now, the Applicants' intentions are not clear.

In addition, the language of claims 64, 240, 259, 278, 297, 314, 333, 352, and 371 is confusing, rendering the claims confusing. On the one hand, one skilled in the art understands that the language of independent claim 64, 240, 259, 278, 297, 314, 333, 352, and 371 "a heterologous cell comprising a nucleic acid molecule encoding SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74" means that the heterologous cell comprises the nucleotides sequence consisting of the start codon before the first codon

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of the nucleotide sequence translated from amino acid sequence of SEQ ID NOs: 43, 58, 59, 60, 67, 68, 69, 70 and 74 and the stop codon immediately after the translated sequence; i.e., one of skills in the art understands that the sequence expressed in the heterologous cell will consists of SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74. On the other hand, the literary meaning covers a heterologous cell comprising any DNA molecule comprising a nucleotide sequence encoding SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74. One of DNA molecules comprising molecules encoding SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74 has already been patented and taught how to be expressed; see the rejection under 35 U.S.C. section 102 bellow. It is important to amend the language of the claims to be precise. As it stands now, the Applicants' intentions are not clear. Please correct the language of the claims.

## **2.2. 35 U.S.C. 102**

### **A. Claims rejected**

Claims 48 and 51-57, claims 114-121, claims 122-129, claims 130-137, claims 138-145 claims, claims 146-153, claims 154-161, claims 162-169 and claims 170-177 are rejected for the reasons explained in the Office Action of March 1, 2005, and December 16, 2005 (previous actions), which are reminded herein. Each set of the claims is directed to

an isolated nucleic acid molecule

expression vector, and

host cell,

wherein the nucleic acid molecule **comprises** a sequence of nucleotides encoding a truncated form of human beta secretase of SEQ ID NO: 2 consisting of 501 amino acids. The claimed truncated forms retain beta-secretase activity and are identified by

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SEQ ID NO: 43 (amino acids 46-501)

SEQ ID NO: 58 (amino acids 46-452)

SEQ ID NO: 59 (amino acids 1-452)

SEQ ID NO: 60 (amino acids 1-420)

SEQ ID NO: 67 (amino acids 58-501)

SEQ ID NO: 68(amino acids 58-452)

SEQ ID NO: 69 (amino acids 63-501)

SEQ ID NO: 70 (amino acids 63-452)

SEQ ID NO: 74 (amino acids 22-452)

In summary, each of the sets of the claims is rejected over Gurney et al., with priority to the provisional application 60/101,594 ('594) filed Sept. 24, 1998 (see SEQ ID NO: 5). As this benefit of the filing date of the '594 provisional application is necessary for Gurney et al. to qualify as prior art under 102(e), the rejection is explained with reference to the provisional application.

'594 discloses also expression of ASP2 in heterologous cells which are bacterial, insect, yeast or mammalian cells; see Example 4, line 15, and specification page 10 line 23, page 11 line 1 and page 11 line 18. '594 teaches also expression vectors useful for transformation; see page 9, line 11, page 10 line 28 and page 11 line 24.

In summary '594 anticipates all what is claimed in the sets of claims as written above.

### Response to Applicants' arguments

Applicants' position is that "Guerney's SEQ ID NO: 5 does not consist of nucleotides encoding present SEQ ID NO: 43. Many other nucleotides encoding other parts of beta secretase are also present in SEQ ID NO: 5 of Guerney", Remarks, page 32, line 4 of the second paragraph.

Firstly, a polymer that is DNA molecule consists of units that are nucleotides. Using the term “nucleotides” to mean nucleotide sequences that encode polypeptides or protein is not proper and confusing. Secondly, although Gurney’s nucleotide sequence set forth by SEQ ID NO: 5, in the provisional application, does not consist of any of DNA molecules encoding truncated forms of SEQ ID NO: 2 listed above, Gurney’s SEQ ID NO: 5 comprises all these DNA molecules. Thus correction of the language of the claims is necessary to place them in condition for allowance; see rejection under 5 USC section 112, second paragraph, above.

**B. Claims not rejected**

Applicants are reminded that  
claims 58-69

claims 178-183 and 240-258

claims 184-189 and 259-277

claims 190-195 and 278-296

claims 196-201 and 297-313

claims 202-207 and 314-332

claims 208-213 and 333-351

claims 214-219 and 352-370

claims 220-225 and 371-389

are not rejected under 35 USC section 102 or 35 USC section 103, because



- 1) it is understood that the language of independent claims 58, 178, 184, 190, 196, 202, 208, 214, 220 "a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 43" means that the vector comprises the nucleotides sequence consisting of the start codon before the first codon of the nucleotide sequence translated from amino acid sequence of SEQ ID NOs: 43, 58, 59, 60, 67, 68, 69, 70 and 74 and the stop codon immediately after the translated sequence; i.e., it is understood that the expressed sequences are consisting of SEQ ID NO:43, 58, 59, 60, 67, 68, 69, 70 and 74
- 2) it is understood that the language of independent claim 64, 240, 259, 278, 297,314, 333, 352, and 371 "a heterologous cell comprising a nucleic acid molecule encoding SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74 " means that the heterogonous cell comprises the nucleotides sequence consisting of the start codon before the first codon of the nucleotide sequence translated from amino acid sequence of SEQ ID NOs: 43, 58, 59, 60, 67, 68, 69, 70 and 74 and the stop codon immediately after the translated sequence. Thus it is understood that the heterologous cell expresses polypeptides consisting of SEQ ID NO: 43, 58, 59, 60, 67, 68, 69, 70 and 74.

The examiner suggests amending the claims accordingly.

**2.4. 35 USC, first paragraph**

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Claim 63, 183, 189, 195, 201, 207, 213, 219 and 225 are rejected under 35 U.S.C. 112, for the reasons explained in the previous Office Actions.

Response to Applicant's argument.

Applicants argue the claims, which recite antibodies lacking significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2, are enabled in the light of disclosure of US Patent 5,721,130 quoted in paragraph [219] of the instant application. The examiner remains unpersuaded, but, indeed, is willing to allow allowable subject matter which covers DNA molecules encoding enzymatically active truncated forms of SEQ ID NO: 2. These forms are novel, and parallel applications 09/724,569; 09/723,722 and 09/724,569 have been already allowed. The examiner, therefore, suggests canceling claims 63, 183, 189, 195, 201, 207, 213, 219 and 225

**2.5. Double patenting rejection**

*Provisional obviousness type double patenting rejection*

Rejection of claims 48, 51-69, and 114-390 is withdrawn because Applicants filed a terminal disclaimer with respect to application 09/724,569. The terminal disclaimer is correct.

Provisional statutory double patenting rejection

Rejection of claim 114, 48, 131, as claiming the same invention as claims 57-60 of the US application No. 09/724,569 is moot because claims 57-60 were cancelled from 09/724569.

**Reply to Applicants' response**

Applicants' do not address the rejection for provisional double patenting issued in the previous Office Action.

**3. Conclusion**

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner

  
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